Human Her2/Neu pro Sequence of c-erbB Her2-CM-CSF immuno Extracellular HER-Human Her-2/neu on Human breast cance

Human Her-2/neu po Human HER2 (ErbB2) Breast cancer asso

HER2/neu amino aci HER2 transgene pla Human HER-2 protei Human Her2 antigen Human Her-2 protei Human Her-2/neu pr

Human heregulin 2 Human tyrosine kin Human HER-2/neu pr

AAE12130 AAB85458 AAG88267

Mouse Her-2/neu ex Mouse Her-2/neu ex Rat HER-2/neu prot Rat Her-2/neu onco

AAM51152

AAB21206

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3373.5 3373.5 3209.5 3209.5

AB21205

Human HER2 recepto DC8scFv-erbB2EC fu Extracellular port

Human ErbB2 oncopr Human ErbB2 extrac

AAMS1145 AAU98923 AAB60408

ABG70753

AAB21200

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Mouse Her-2/neu pr Amino acid sequenc Mouse Her-2/neu on Rat HER-2/neu prot Rat Her-2/neu onco

Truncated HER-2, p Human p68HER-2 gen Human truncated HE

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Human HER-2/neu fu
Her-2/neu extracel
Human HER-2/neu fu
Human HER-2/neu pr
Human HER-2/neu pr
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Human HER-2/neu on
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Amino acid sequenc
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3196.087 Million cell updates/sec
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GenCore version 5.1.6
(c) 1993 - 2003 Compugen Ltd.
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Listing first 45 summaries
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AAW01111
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AAB21208
AAW92406
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                                                                                                      - protein search, using sw model
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Gapop 10.0 , Gapext 0.5
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A R R S S U S A K K K K K K K K K K K K K K K K K K	321	(D AAB21204 standard; protein; 712 AA.	×	NC AAB21204;		OT 12-JAN-2001 (first entry)		DE Human HER-2/neu fusion protein.		(W Human; HER-2/neu; oncogene; tyrosine kinase; cytostatic; vaccine;			,	оз ношо варієнв.		<b>x</b>	N W0200044899-A1.		pp 03-AUG-2000.		PF 28-JAN-2000; 2000WO-US02164.		PR 29-JAN-1999; 99US-0117976.			PA (SMIK ) SMITHKLINE BEECHAM.		i Cheever MA, Gheysen D;	
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AAM51149

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domain and a preferred portion of the phosphorylation domain of the human receptor-like glycoproteins and shows homology to the epidermal growth factor receptor (EGFR). It probably plays a part in cell growth and/or differentiation. The HER-2/neu gene is an oncogene. HER-2/neu fusion proteins may be used to treat or prevent cancer by eliciting or enhancing an immune response to the HER-2/neu protein. They may be used to treat an animaune area or the HER-2/neu protein. They may be used to treat an animanne as breast, oolon, lung and prostate cancers, and may be used as an antigen to vaccinate against these neoplasias.
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HER-2/neu extracellular domain/phosphorylation domain fusion proteins useful for vaccinating against breast, ovarian, colon, lung and
                                                                                                                                                                                                                                                                                                                                                                                                                                          1 MELAALCRWGLLLALLPPGAASTQVCTGTDMKLRLPASPETHLDMLRHLYQGCQVVQGNL
                                                                                                               present sequence is a fusion protein comprising the extracellular
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The present sequence is that of a fusion protein between the extracellular domain and a fragment (DeltaPD) of the phosphorylation domain of human Her-2/neu (see AAM51143), an oncogenic self-protein and target for anti-cancer vaccines. The fusion protein can be cotained by recombinant DNA methods. Her-2/neu overexpression correlates with a poor prognosis in breast and ovarian cancers. The invention provides Her-2/neu fusion proteins, nucleic acids encoding them, viral vectors, and vaccines comprising the fusion proteins or nucleic acids encoding them, viral vectors, and vaccines comprising the fusion proteins or nucleic acid molecules. In preferred fusion proteins, the extracellular domain of Her-2/neu is fused to a Her-2/neu intracellular domain of Her-2/neu is fused to a Her-2/neu intracellular domain of Her-2/neu is fused to a Her-2/neu citrament). An immune response to Her-2/neu protein is elicited or chanced by administering the fusion protein in the form of a vaccine, or by transfecting cells of an animal ex vivo with a nucleic acid encoding the fusion protein, and delivering the transfected cells corpered to the animal. The fusion protein, nucleic acids, and isolated specific T-cells are useful for inhibiting the development of a cancer, especially breast, ovarian, colon, lung or prostate cancer in a patient. Tells that specifically react with a Her-2/neu corder to inhibit the development of cancer in a patient.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Her-2/neu fusion protein for treating or preventing cancer by eliciting or enhancing an immune response to the protein, has Her-2/neu extracellular domain fused to Her-2/neu intracellular or
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                                                                                                                 Her-2/neu extracellular domain-delta-phosphorylation domain fusion.
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0
                                                                                                                                                   Her-2/neu; oncogene; cancer; tumour; vaccine; human; p185;
tyrosine kinase; receptor; c-erbB2; gene therapy.
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                                                                                                                                                                                                                                                                                                                               'note= "phosphorylation domain fragment"
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Pred. No. 4.2e-299;
Mismatches 0;
                                                                                                                                                                                                                                                                         /note= "extracellular domain"
654..712
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                                                                                                                                                                                                                                                     Location/Qualifiers
AAM51149 standard; Protein; 712 AA
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The present sequence is that of a fusion protein between the extracellular domain and phosphorylation domain of human Her-2/neu (see AAMS1143), an oncogenic self-protein and target for anti-cancer vaccines. The fusion protein can be obtained by recombinant DNA methods. Her-2/neu overexpression correlates with a poor prognosis in breast and ovarian cancers. The invention provides Her-2/neu fusion proteins, nucleic acids encoding them, viral vectors, and vaccines comprising the fusion proteins or nucleic acid molecules. In preferred fusion proteins, the extracellular domain of a Her-2/neu protein is fused to a Her-2/neu intracellular domain or phosphorylation domain (or its DeltaPD fragment). An immune therophorylation domain protein is elicited or enhanced by administering the fusion protein in the form of a vaccine, or by transfecting cells of an animal ex vivo with a nucleic acid encoding the fusion protein, and delivering the transfected cells to the animal. The fusion proteins, nucleic acids, and isolated specific 7-cells are useful for inhibiting the development of a cancer, especially breast, ovarian, colon, lung or prostate cancer in a patient. T cells that specifically react with a Her-2/neu fusion protein can be used to remove tumour cells from a sample in corder to inhibit the development of cancer in a patient.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Her-2/neu fusion protein for treating or preventing cancer by eliciting or enhancing an immune response to the protein, has Her-2/neu extracellular domain fused to Her-2/neu intracellular or
Her-2/neu extracellular domain-phosphorylation domain fusion
                                                                                                                                                                                                                                                 Her-2/neu; oncogene; cancer; tumour; vaccine; human; p185;
tyrosine kinase; receptor; c-erbB2; gene therapy.
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/note= "extracellular domain"
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Score 3954; DB 23; Length 919; Pred. No. 6e-299;

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Best Local Similarity

Query Match

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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      HER-2/neu; c-erbB1; p185; oncogene; tyrosine protein kinase; breast cancer; ovary cancer; colon cancer; lung cancer; prostate cancer; immunisation; tumour; vaccine; vector.
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                                                                                                                                                                                                                                                                                        HER-2/neu extracellular domain/phosphorylation domain fusion proteins useful for vaccinating against breast, ovarian, colon, lung and
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Pred. No. 6.2e-285;
); Mismatches 0;
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29-JAN-1999;
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                                            Human HER-2/neu protein (AAW01111), also called p185 or c-erbB2, is the product of the HER-2/neo oncogene (see also AAT40739). The product of early pressed in various cancers, including breast, over-appressed in various cancers, including breast, protein can be used to immunise an animal against a malignancy with which the oncogene is associated. The polypeptide can be produced in transformed host cells for use in immunisation. Alternatively, animal cells are transfected in vivo or ex vivo with a viral vector that directs expression of the polypeptide.
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Pred. No. 6.6e-285;
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               Page 56-61; 71pp; English
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781 YVSRLLGICLTSTVQLVTQLMPYGCLLDHVRENRGRLGSQDLLNWCMQIAKGMSYLEDVR
                                         841 LVHRDLAARNVLVKSPNHVKITDFGLARLLDIDETEYHADGGKVPIKWMALESILRRRFT
                                                                                    901 HQSDVWSYGVTVWELMTFGAKPYDGIPAREIPDLLEKGERLPQPPICTIDVYMIMVKCWM
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                                                                                                                                                                                                                                                                                                                 cell; immunisation;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Use of HER-2/neu polypeptides - for an HER-2/neu associated malignancy, preventing tumours
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The present sequence is the human HER-2/neu protein. It is a member of the tyrosine kinase family of receptor-like glycoproteins and shows homology to the epidermal growth factor receptor (EGFR). It probably plays a part in cell growth and/or differentiation. The HER-2/neu gene is an oncogene. An HER-2/neu fusion protein comprising a HER-2/neu extracellular domain fused to a HER-2/neu phosphorylation domain may be used to treat or prevent cancer by eliciting or enhancing an immune response to the HER-2/neu protein. It may be used to treat malignancies such as breast, ovarian, colon, lung and prostate cancers, and may be used as an antigen to vaccinate against
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Pred. No. 6.6e-285;
0; Mismatches 0;
 1021 EEYLVPQQGFFCPDPAPGAGGMVHHRHR 1048
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                                                                    AAB21198 standard; protein; 1255
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Best Local Similarity 67.9%;
Matches 712; Conservative
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                                                                                                                                                  Human HER-2/neu protein.
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N-PSDB; AAA89736.
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                                                                                                                                                                                                                                                                                                                                                            The present sequence represents a SPLICE erbB-2 receptor protein. The protein has an in-frame deletion of 16 amino acids, 2 of which are conserved cysteine residues, compared to the unspliced protein. The erbB-2 polymucleotide is used to construct probes for detecting disorders of cell transformation such as cancer. Antibodies to the protein may be used to detect SPLICE erbB-2 in a sample. Agents (e.g. antisense oligonucleotides) which inhibit the expression of SPLICE erbB-2 are useful for reducing tumor cell proliferation and treating cancer. Substances which stimulate SPLICE erbB-2 are useful for treating conditions involving damaged cells including conditions in which degeneration of tissue occurs, such as arthropathy, beneresorption, inflammatory diseases, degenerative disorders of the central nervous system and wound healing.
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                                                                                                                                                                                                                                                                                    Nucleic acid encoding an erbB 2 receptor protein designated SPLICE erbB-2, inhibitors of the protein are useful for treatment of cancer
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nes 712; Conservative
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LTLIDTNRSRACHPCSPMCKGSRCWGESSEDCQSLTRTVCAGGCARCKGPLPTDCCHEQC 240
                                                241 AAGCTGPKHSDCLACLHFNHSGICELHCPALVTYNTDTFESMPNPEGRYTFGASCVTACP
                                                                                                             301 YNYLSTDVGSCTLVCPLHNQEVTAEDGTQRCEKCSKPCARVCYGLGMEHLREVRAVTSAN
                                                                                                                                                                              361 IQEFAGCKKIFGSLAFLPESFDGDPASNTAPLQPEQLQVFETLEEITGYLYISAWPDSLP
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                               AAGCTGPKHSDCLACLHFNHSGICELHCPALVTYNTDTFESMPNPEGRYTFGASCVTACP
                                                                                             YNYLSTDVGSCTLVCPLHNQEVTAEDGTQRCEKCSKPCARVCYGLGMEHLREVRAVTSAN
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DLSVFONLQVIRGRILHNGAYSLTLQGLGISWLGLRSLRELGSGLALIHHNTHLCFVHTV PWDQLFRNPHQALLHTANRPEDECVGEGLACHQLCARGHCWGPGPTQCVNCSQFLRGQEC	VERCHUGGEREYUNAHCLEPCHECOPONGSYTCFGEBOOCYACAHYKDPPFCVARC	601 PSGVKPDLSYMPIWKFPDEEGACQPCPINCTHSCVDLDDKGCPAEQRASPLTSIISAVVG 660 654 653 661 ILLVVVLGVVFGILIKRRQQXIRKYTWRRLLQETELVEPLTPSGAMPNQAQMRILKETEL 720 654	721 RKVKVLGSGAFGTVYKGIWIPDGENVKIPVAIKVLRENTSPKANKEILDEAYVMAGVGSP 780 654	841 LVHRDLAARNVLVKSPNHVKITDFGLARLLDIDETEYHADGGKVPIKWMALESILRRRFT 900 654	INFILITION INFINITION INFILITION	<pre>ILT 10 12620 AAY92620 standard; Protein; 1255 AA. AAY92620;</pre>	10-AUG-2000 (first entry) Human heregulin 2 (Her2).	Heregulin 2; Her2; vaccination; cytotoxic T-lymphocyte immunity; self-protein; cancer; breast cancer; prostate cancer; cell-associated peptide antigen; foreign epitope.	Key Location/Qualifiers  Domain 1173  /label= N-terminal  /note= "mature polypeptide"  Region 526  /label= insertion region	/ince== insection region  /note= "guitable for foreign epitope insertion"  5973 /label= insertion region /note= "guitable for foreign epitope insertion"  Region 10317	

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961 IDSECRPRFRELVSEFSRMARDPQRFVVIQNEDLGPASPLDSTFYRSLLEDDDMGDLVDA 1020
                      RKVKVLGSGGAFGTVYKGIWIPDGENVKIPVAIKVLRENTSPKANKEILDEAYVMAGVGSP 780
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Novel synthetic therapeutic compound for inducing immune response and for use in adoptive immunotherapy, has enhanced binding to major histocompatibility molecules and enhanced immunoregulatory properties
                                                                                                             781 YVSRLLGICLTSTVQLVTQLMPYGCLLDHVRENRGRLGSQDLLNWCMQIAKGMSYLEDVR
                                                                                                                                                                                               841 LVHRDLAARNVLVKSPNHVKITDFGLARLLDIDETEYHADGGKVPIKWMALESILRRRFT
                                                                                                                                                                                                                                                                                      901 HQSDVWSYGVTVWELMTFGAKPYDGIPAREIPDLLEKGERLPQPPICTIDVYMIMVKCWM
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Therapeutic compound; major histocompatibility complex; vaccine; antigenic peptide; MHC; immunoregulatory; immune response; HER-2; adoptive immunotherapy; anti-cancer; breast cancer antigen; APC; antigen presenting cell; human; tyrosine kinase-type receptor.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Human tyrosine kinase-type receptor, HER-2.
                                                                                                                                                                                                                                                                                                                                                                                                                                                      1021 EEYLVPQQGFFCPDPAPGAGGWVHRHR 1048
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immunogenized forms. Regions suitable for the insertion of foreign T helper epicopses were identified (see features table). The method is used for inducing immune responses against weakly immunogenic cell-associated peptide antigens (PA) such as those associated with cancers (self-proteins), e.g. human prostate specific membrane antigens (PSM), heregulin 2 (Her2) and/or fibroblast growth factor 8b (FGF8b). The method comprises effecting simultaneous presentation by antigen producing cells (APCB) of the animals immune system of: (1) at least 1 cTL (Cytotoxic T-lymphocyte) group derived from the PA and/or at least 1 B-cell group derived from the cell-associated PA, and (2) at least 1 first T helper cell group which is foreign to the animal. Analogues of human PSM, human Herz and human/murine FGF8b comprising a substantial part of all known and predicted CTL and B-cell epitopes of the respective PA and including at least one foreign T helper epitope are also claimed. The method is used to treat prostate, prostate, breast cancer the part of the part of the prostate of prostate or breast cancer the part of the part of the prostate of prostate or breast cancer the part of the part of the prostate of prostate or breast cancer the part of the part of the prostate or prostate or present cancer the part of the part of the prostate or prostate the part of present cancer the part of the part of the prostate or present cancer the part of the part of the prostate or present cancer the part of the part of the prostate cancer the part of the part of the prostate the part of the part of the part of the part of the prostate the prostate the part of the
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Pred. No. 6.6e-285;
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Best Local Similarity 67.9
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                       341 LVHRDLAARNVLVKSPNHVKITDFGLARLLDIDETEYHADGGKVPIKWMALESILRRRFT
                                                                                                              901 HQSDVWSYGVTVWELMTFGAKPYDGIPAREIPDLLEKGERLPQPPICTIDVYMIMVKCWM
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cytostatic; vaccine; p185;
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                  characterised by expression of the breast cancer antigen, HER-2. Polynucleotides that encode peptides of the invention are useful as hybridisation probes and as primers for the detection of genes of gene transcripts that are expressed in antigen presenting cells (APCs), to confirm transduction of polynucleotides into host cells. The present sequence is human tyrosine kinase-type receptor, HER-2. Compounds of the invention are designed based on the HER-2 antigenic peptide
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                                                                                                                                                                                                                                                                                                                         Gaps
    expand immune effector cells that are specific for cancers
                                                                                                                                                                                                                                                                                                                    Indels 336;
                                                                                                                                                                                                                                                                            Length 1255
                                                                                                                                                                                                                                                                       Score 3776; DB 22;
Pred. No. 6.6e-285;
0; Mismatches 0;
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Best Local Similarity 67.9'
Matches 712; Conservative
                                                                                                                                                                                                                               1255 AA;
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HER-2/neu;

us-09-854-356-7.rag

3 120	A 180 A 180	C 240	. 300 d	N 360 	P 420	V 480   480 V 480	C 540 C 540	009 C	- 653 G 660	- 653	L 720	- 653	P 780	- 653	R 840	- 653	T 900	- 653	M 960	A 684	A 1020	2
	DPLNNTTPVTGASPGGLRELQLRSLTEILKGGVLIQRNPQLCYQDTILWKDIFHKNNQLA 	LTLIDTNRSRACHPCSPMCKGSRCWGESSEDCQSLTRTVCAGGCARCKGBLPTDCCHEQC 	AAGCTGPKHSDCLACLHFNHSGICELHCPALVTYNTDTFESMPNPEGRYTFGASCVTACP	YNYLSTDVGSCTLVCPLHNQEVTAEDGTQRCEKCSKPCARVCYGLGMEHLREVRAVTSAN 	IQEFAGCKKIFGSLAFLPESFDGDPASNTAPLQPEQLQVFETLEEITGYLYISAWPDSLP 	DLSVPONLOVIRGRILHNGAYSLTLOGIGISWLGLRSLRELGSGLALIHHNTHLCFVHTV 	PWDQLFRNPHQALLHTANRFEDECVGEGLACHQLCARGHCWGPGPTQCVNCSQFLRGQEC 	VEECRVLQGLPREYVNARHCLPCHPECQPQNGSVTCFGPEADQCVACAHYKDPPFCVARC	PSGVKPDLSYMPIWKEPDEEGACQPCPINCTHSCVDLDDKGCPAEQRASPLTS                     psgvkpdlsympiwkepdeegacQpcpincTHScvDlddkgcPaeQRaspltsisavvg		ILLVVVLGVVFGILIKRRQQKIRKYTMRRLLQETELVEPLTPSGAMPNQAQMRILKETEL		RKVKVLGSGAFGTVYKGIWI PDGENVKI PVAIKVLRENTSPKANKEILDEAYVMAGVGSP		YVSRLLGICLTSTVQLVTQLMPYGCLLDHVRENRGRLGSQDLLNWCMQIAKGMSYLEDVR		LVHRDLAARNVLVKSPNHVKITDFGLARLLDIDETEYHADGGKVPIKWMALESILRRRFT		HQSDVWSYGVTVWELMTFGAKPYDGIPAREIPDLLEKGERLPQPPICTIDVYMIMVKCWM	QNEDLGPASPLDSTFYRSLLEDDDMGDLVD	IDSECRPRFRELVSEFSRMARDPQRFVVIQNEDLGPASPLDSTFYRSLLEDDDMGDLVDA	-HRHR 712          -HRHR 1048
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AAG88267 standard; Protein; 1255 AA.

RESULT 13
AAG88267
ID AAG88
XX
AC AAG88

AAG88267

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The present invention describes isolated prepared HER2/neu epitopes (I).

Also described are: (1) a clonal cytotoxic T lymphocyte (CTL) that is

CC culture in vitro and binds to a complex of an epitope (I), bound to a

culture in vitro and binds to a complex of an epitope (II) bound to a

culture composition (HLA) molecule; (2) a peptide (II) comprising (I)

and a second epitope and the peptide is less than 50 contiguous amino

cc acids that have 100% identity with a native peptide sequence of HERZ/neu;

(3) a vaccine composition (III) comprising (II) and a pharmaccutical

cxcipient; (4) an isolated nucleic acid encoding a peptide comprising

(I); and (5) an isolated nucleic acid encoding (II) (I) has cytostatic

cand immunostimilant activities, and can be used in vaccines (I), (II)

and (III) are useful for inducing cellular immune responses for the

prevention and treatment of cancer. (I) and (II) are useful for

complexing or evaluating an immune response to a tumour-associated

antigen when incubated with a T lymphocyte to (I) or (II). Epitope

cc antigen when incubated with a T lymphocyte to (I) or (II). Epitope

cc antigen when incubated with a T lymphocyte to (I) or (II). Epitope

cc antigen sean that immunosuppressive epitopes may be combined to

in whole antigens may be avoided. Selected epitopes may be combined to

content immunogenicity. The possible pathological side effects caused by

infectious agents or whole protein antigen is eliminated. The vaccine

convoides the ability to direct and focus an immune response to multiple

convoides the opportunity to combine epitopes derived from

cultiple tumour-associated molecules addressing the problem of tumour

cumultiple tumour-associated molecules and immune response to multiple

culture variability and reducing the likelihood of tumour escape due to

cutumour variability and reducing the likelihood of tumour escape due to

cutumour variability end precent invention.
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                                                                                                        Human; HER2/neu; epitope; human leukocyte antigen; HLA; T cell; immune response; vaccine; tumour; cancer; cytostatic; immunostimulant; tumour-associated antigen; T lymphocyte; cytotoxic T lymphocyte; CTL.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     An isolated prepared HER2/neu epitope useful in a vaccine for inducing cellular immune responses for the prevention and treatment of cancer -
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       1 MELAALCRWGLLLALLPPGAASTQVCTGTDMKLRLPASPETHLDMLRHLYQGCQVVQGNL
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  1 MELAALCRWGLLLALLPPGAASTQVCTGTDMKLRLPASPETHLDMLRHLYQGCQVVQGNL
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Indels 336; Gaps
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Sette A, Sidney J, Southwood S, Chesnut R, Celis E;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        95.5%; Score 3776; DB 22; Length 1255; 67.9%; Pred. No. 6.6e-285; ive 0; Mismatches 0; Indels 336;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Disclosure; Page 15; 199pp; English.
                                                                   HER2/neu amino acid sequence.
                                                                                                                                                                                                                                                                                                                                                                                                 99US-0458299.
                                                                                                                                                                                                                                                                                                                                                   11-DEC-2000; 2000WO-US33591.
                     (first entry)
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nes 712; Conservative
                                                                                                                                                                                                                                                                                                                                                                                                                                               (EPIM-) EPIMMUNE INC.
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                                                                                                                                                                                                           Homo sapiens.
                                                                                                                                                                                                                                                                                                                                                                                                 10-DEC-1999;
                                                                                                                                                                                                                                                                                                       14-JUN-2001.
                     11-SEP-2001
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Keogh E;
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Matches
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DLSVPONLQVIRGRILHNGAYSLTLGGLGISWLGLRSLRELGSGLALTHNYHLCPVHTV 480
                                                                                                                                                                                                                                                                                                                                                      The present invention provides a method of treating cancer by administering a conjugate of anti-ErbB antibody with a maytansinoid. In particular, the antibody is directed against ErbB2 (also known as HER2 and pl85neu). The method is particularly useful in the treatment of breast, ovarian, stomach, endometrial, salivary gland, lung, kidney, colon, colorectal, thyroid, pancreatic, prostate and bladder cancers.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 ELTYLPTNASLSFLQDIQEVQGYVLIAHNQVRQVPLQRLRIVRGTQLFEDNYALAVLDNG
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  LTLIDTNRSRACHPCSPMCKGSRCWGESSEDCOSLTRTVCAGGCARCKGPLPTDCCHEOC
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  AAGCTGPKHSDCLACLHFNHSGICELHCPALVTYNTDTFESMPNPEGRYTFGASCVTACP
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                YNYLSTDVGSCTLVCPLHNQEVTAEDGTQRCEKCSKPCARVCYGLGMEHLREVRAVTSAN
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               IQEFAGCKKIFGSLAFLPESFDGDPASNTAPLQPEQLQVFETLEEITGYLYISAWPDSLP
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              MELAALCRWGLLLALLPPGAASTQVCTGTDMKLRLPASPETHLDMLRHLYQGCQVVQGNL
             cancer;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Gaps
                                                                                                                                                                                                                                                                              Treating tumors, particularly breast cancers, which overexpress an receptor and does not respond to an anti-ErbB antibody, comprises conjugating the antibody to a maytansinoid -
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Indels 336;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Length 1255;
             conjugate;
            receptor; pl85neu; maytansinoid
                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Score 3776; DB 22;
Pred. No. 6.6e-285;
0; Mismatches 0;
                                                                                                                                                                                                                                                                                                                                 Example 3; Fig 4; 92pp; English
                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Match 95.5%;
Local Similarity 67.9%;
Les 71.2; Conservative 0
                                                                                                                                                         25-JUN-1999; 99US-0141316.
16-MAR-2000; 2000US-0189844.
                                                                                                                                  2000WO-US17229
                                                                                                                                                                                             (GETH ) GENENTECH INC
                                                                                                                                                                                                                     Schwall
                                                                                                                                                                                                                                              2001-061962/07.
            HER2; ErbB2
                                                                                                                                                                                                                                                                                                                                                                                                                                            1255 AA
                                                                                                                                                                                                                                                          N-PSDB; AAF24297
                                                                                  WO200100244-A2
                                              Homo sapiens.
Synthetic.
                                                                                                                                  23-JUN-2000;
                                                                                                                                                                                                                     Erickson S,
                                                                                                         04-JAN-2001
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                                                                                                         The invention relates to a transgenic non-human mammal that produces in its mammary gland cells detectable levels of a native human HER2 protein or its fragment. The transgenic animals are useful as tumour models for testing HER2-directed cancer therapies, and for identifying anticancer agents. The animals may also be used as source of cells which can be immortalised in culture, in screening for compounds that have potential as prophylactic or therapeutic treatments of diseases or disorders involving expression of HER2. The anti-cancer molecules are useful for inducting apoptosis or cell death of cancer cells. The present sequence is human HER-2 protein.
       nnsgenic non-human mammal that produces detectable levels of a human HER2 protein in its mammary gland cells, useful as tumor for testing HER2-directed cancer therapies, and for identifying
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cancer; therapy; apoptosis; cytostatic; human.
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Human tyrogine kin HER2 transgene pla Human HER-2 protei Human HER2 antigen Human HER2 (ErbB2)

Breast cancer asso Human Her2/Neu pro Sequence of c-erbB Human breast cance

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Title: Perfect score:

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Scoring table:

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Human; HER-2/neu; oncogene; tyrosine kinase; cytostatic; vaccine; breast cancer; prostate cancer; ovarian cancer; lung cancer; colon cancer; fusion protein.
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 29-JAN-1999; 99US-0117976
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(SMIK ) SMITHKLINE BEECHAM.
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 Cheever MA, Gheysen D;
 WO200044899-A1.
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Synthetic.
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             GenCore version 5.1.6
(c) 1993 - 2003 Compugen Ltd.
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HER-2/neu extracellular domain/phosphorylation domain fusion proteins useful for vaccinating against breast, ovarian, colon, lung and
                                                                                                                                                                                                                                                                                                                                                           1 MELAALCRWGLLLALLPPGAASTQVCTGTDMKLRLPASPETHLDMLRHLYQGCQVVQGNL
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                                                                                        The present sequence is a fusion protein comprising the extracellular domain and the phosphorylation domain of the human HER-2/neu protein. HER-2/neu is a member of the tyrosine kinase family of receptor-like
                                                                                                                                                                                                                                                                                                                              Gaps
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                                                             Claim 2; Fig 12; 128pp; English.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       eliciting
                                                  TVPLPSETDGYVAPLTCSPQPEYVNQPDVRPQPPSPREGPLPAARPAGATLERPKTLSPG
                                 TVPLPSETDGYVAPLTCSPQPEYVNQPDVRPQPPSPREGPLPAARPAGATLERPKTLSPG
                                                                                                   KNGVVKDVFAFGGAVENPEYLTPQGGAAPQPHPPPAFSPAFDNLYYWDQDPPERGAPPST
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Her-2/neu fusion protein for treating or preventing cancer by or enhancing an immune response to the protein, has Her-2/neu extracellular domain fused to Her-2/neu intracellular or
                                                                                                                                                                                                                                                                                                                                                                                          Her-2/neu extracellular domain-phosphorylation domain fusion.
                                                                                                                                                                                                                                                                                                                                                                                                                           Her-2/neu, oncogene, cancer, tumour, vaccine, human, p185, tyrosine kinase, receptor, c-erbB2, gene therapy.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              /note= "phosphorylation domain"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             'note= "extracellular domain"
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(SMIK ) SMITHKLINE BEECHAM BIOLOGICALS.
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to the animal. The fusion proteins, nucleic acids, and isolated specific T-cells are useful for inhibiting the development of a cancer, especially breast, ovarian, colon, lung or prostate cancer in a patient. T cells that specifically react with a Her-2/neu fusion protein can be used to remove tumour cells from a sample in
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                                                                                                Length 919;
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                                                    order to inhibit the development of cancer in a patient
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           immunisation"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              HER-2-neu poly;peptide(s) - used for prevention or malignancies with which the HER-2/neu oncogene is
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                                                                                                                                                                                                                                                                                                                                                                                                      HER-2/neu; c-erbB1; p185; oncogene; tyrosine protein kinase; breast cancer; ovary cancer; colon cancer; lung cancer; prostate cancer; immunisation; tumour; vaccine; vector.
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/label= Intracellular domain
/note= "claimed domain, useful for
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                                                                                                                                                                                         AAW01111 standard; Protein; 1255
919
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Matches 919; Conservative
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2406 standard; Protein; 1255 AA.

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241 AAGCTGPKHSDCLACLHFNHSGICELHCPALVTYNTDTFESMPNFEGRYTFGASCVTACP	301 YNYLSTDVGSCTLVCPLHNQEVTAEDGTQRCERCSRPCARVCYGLGMEHLREVRAVTSAN		541 VEECKVLOGLEKEYNAKHCLECHFECOLONGSVTCFGFEADOCVACAHYKDPFFCVARC 541 VEECRVLOGLEREYNARHCLECHFECOLONGSVTCFGFEADOCVACAHYKDPFFCVARC 601 PSGVKPDLSYMPIWKEPDEEGACOPCPINCTHSCVDLDDKGCPAEQRASPLTS 601 PSGVKPDLSYMPIWKPPDEEGACOPCPINCTHSCVDLDDKGCPAEQRASPLTS	661 ILLVVVLGVVFGILIKRRQQKIRKYTMRRLLQETELVEPLTPSGAMPNQAQMRILKETEL 654 ************************************	721 RKVKVLGSGAFGTVYKGIWIPDGENVKIPVAIKVLRENTSPKANKEILDEAYVMAGVGS 654	781 YVSRLLGICLTSTVQLVTQLMPYGCLLDHVRENRGRLGSQDLLNWCMQIAKGMSYLEDVR 654	654	654	745 AGSDVFDGDLGMGAAKGLOSLPTHDPSPLQRYSEDPTVPLSETDGYVAPLTCSPQPEYV	201 GGAAPQPHPPPAFSPAFDNLYYWDQDPPERGAPPSTFKGTPTAENPEYLGLDVP

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sequence represents the human HER-2/neu oncogene protein. A fragment this protein is used in a method for eliciting or enhancing an immune sonse to HER-2/neu protein. The polypeptide can stimulate T cells and talls to produce an immune response to the HER-2/neu protein. The loca can be used for immunisation against a malignancy in which the 2/neu oncogene is associated and in the treatment of an existing our, or to prevent tumour occurrence or reoccurrence.
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                                                                                                                                        2/neu, oncogene; immune response; T cell; B cell; immunisation;
gnancy; treatment; tumour.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       of HER-2/neu polypeptides - for eliciting an immune response ER-2/neu associated malignancy, particularly for treating or
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       atch 96.5%; Score 4900; DB 20; Length 1255; cal Similarity 73.2%; Pred. No. 0; 919; Conservative 0; Mismatches 0; Indels 336;
                                                                                                                                                                                                                                                            Location/Qualifiers
676..1255
/note= "region which elicits immune response"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       m 3; Column 31-38; 26pp; English.
                                                                                           n HER-2/neu oncogene protein.
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93US-0033644.
93US-0106112.
95US-0414417.
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ELTYLPTNASLSFLODIQEVQGYVLIAHNOVRQVPLQRLRIVRGTQLFEDNYALAVLDNG 120
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                                                                                                        HER-2/neu; oncogene; tyrosine kinase; cytostatic; vaccine; cancer; prostate cancer; ovarian cancer; lung cancer;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               HER-2/neu extracellular domain/phosphorylation domain fusion useful for vaccinating against breast, ovarian, colon, lung a prostate cancers -
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73.2%; Pred. No. 0;
ive 0; Mismatches
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Matches 919; Conservative
                                                    Human HER-2/neu protein.
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12-JAN-2001
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SPLICE erbB-2 receptor protein; cell transformation disorder; tumor cell proliferation; tissue degeneration; arthropathy; bone resorption; inflammatory disease; degenerative disorder; wound healing.

99WO-CA00912 98US-0165192.

01-OCT-1999; 02-OCT-1998;

13-APR-2000

WO200020579-A1 Homo sapiens.

Muller WJ, Siegel PM; (UYMC-) UNIV MCMASTER

WPI; 2000-303768/26.

N-PSDB; AAA14812

Amino acid sequence of the SPLICE erbB-2 receptor protein.

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The present sequence represents a SPLICE erbB-2 receptor protein. The protein has an in-frame deletion of 16 amino acids, 2 of which are conserved cysteine residues, compared to the unspliced protein. The erbB-2 polymucleotide is used to construct probes for detecting disorders of cell transformation such as cancer. Antibodies to the protein may be used to detect SPLICE erbB-2 in a sample. Agents (e.g. antisense oligonucleotides) which inhibit the expression of SPLICE erbB-2 are useful for reducing tumor cell proliferation and treating cancer. Substances which stimulate SPLICE erbB-2 are useful for treating conditions involving damaged cells including conditions in which degeneration of tissue occurs, such as arthropathy, bone resorption, inflammatory diseases, degenerative disorders of the central nervous system and wound healing.
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                            YNYLSTDVGSCTLVCPLHNQEVTAEDGTQRCEKCSKPCARVCYGLGMEHLREVRAVTSAN
                                                                                 EEYLVPQQGFFCPDPAPGAGGMVHHRHRSSSTRSGGGDLTLGLEPSEEEAPRSPLAPSEG
               YNYLSTDVGSCTLVCPLHNQEVTAEDGTQRCEKCSKPCARVCYGLGMEHLREVRAVTSAN
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receptor protein. The

Nucleic acid encoding an erbB 2 receptor protein designated SPLICE erbB-2, inhibitors of the protein are useful for treatment of cancer

Claim 3; Fig 2; 60pp; English.

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ELTYLPTNASLSFLQDIQEVQGYVLIAHNQVRQVPLQRLRIVRGTQLFEDNYALAVLDNG 120
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AAY84780 standard; Protein; 1255

08-AUG-2000 (first entry)

AAY84780;

RESULT 6
AAY84780
ID AAY8
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DT 08-A

240 240 300 300

180

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The invention provides an isolated antigen-presenting cell, which expresses at least an immunogenic portion of a polypeptide that produces an immune response to HER-2/neu protein. The antigen-presenting cells are useful as vaccines for eliciting or enhancing an immune response to HER-2/neu protein, particularly in treating or preventing malignancies in which the HER-2/neu oncogene is associated. Specifically, these are useful for treating or preventing cancer, e.g. breast cancer, ovarian, colon, lung or prostate cancers. The present sequence represents the human HER-2/neu protein (also known as p185 or c-erbB2).
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Gaps

Indels 336; Length 1255;

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An isolated prepared HER2/neu epitope useful in a vaccine for inducing cellular immune responses for the prevention and treatment of cancer -

Disclosure; Page 15; 199pp; English.

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Celis

Chesnut R,

Southwood S,

Sette A, Sidney J,

Fikes J, Keogh E;

Keogh

WPI; 2001-374995/39.

(EPIM-) EPIMMUNE INC

11-DEC-2000; 2000WO-US33591.

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Human; HER2/neu; epitope; human leukocyte antigen; HLA; T cell; immune response; vaccine; tumour; cancer; cytostatic; immunostimulant; tumour-associated antigen; T lymphocyte; cytotoxic T lymphocyte; CTL. Ā AAG88267 standard; Protein; 1255 HER2/neu amino acid sequence. (first entry) WO200141787-A1 11-SEP-2001 AAG88267;

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14-JUN-2001

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The present invention describes isolated prepared HER2/neu epitopes (I). Also described are: (I) a clonal cytotoxic T lymphocyte (CTL) that is culture in vitro and binds to a complex of an epitope (II), bound to a human leukocyte antigape (HIA) molecule; (2) a peptide (II) comprising (I) and a second epitope and the peptide is less than 50 contiguous amino caids that have 100% identity with a native peptide sequence of HER2/neu; (3) a vaccine composition (III) comprising (II) and a pharmaceutical excipient; (4) an isolated nucleic acid encoding a peptide comprising (I); and (5) an isolated nucleic acid encoding (II). (I) has cytostatic and immunostimilant activities, and can be used in vaccines (I), (II) are useful for inducing cellular immune response for the prevention and treatment of cancer. (I) and (III) are useful for inducing cellular immune response for the prevention and treatment of cancer. (I) and (II) are useful for antigen when incubated with a T lymphocyte sample form a patient and electing the presence of bound T lymphocyte sample form a patient and electing the presence of bound T lymphocyte sample form a patient of contines mean that immunosuppressive epitopes may be combined to inhere immunogenicity. The possible pathological side effects caused by infectious agents or whole protein antigen is eliminated. The vaccine provides the ability to direct and focus an immune response to multiple cumour-associated molecules addressing the problem of tumour cumour variability and reducing the likelihood of tumour escape due to antigen loss. AAG88266 to AAG89121 represent amino acid sequences used in the exemplification of the present invention.
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The invention relates to antisense compounds targetted to a nucleic acid molecule encoding Her2 (human Epidermal Growth Factor receptor 2) that specifically hybridises with and inhibits the expression of Her2. Antisense compounds of the invention are used for treating diseases or conditions associated with Her2 such as hyperproliferative diseases or e.g. lung, breast, gastric, oesophageal, colon, bladder, salivary, neural or cardiac cancer. They are also useful prophylactically e.g. to prevent or delay infection, inflammation and tumnour formation. The invention is also used in gene therapy. The present sequence is human
                                                                                                                                                                                                                    Novel antisense oligonucleotide which modulates the ex
Epidermal Growth Factor receptor, Her2, is useful for
inflammation or to prevent infection in humans -
  tumour; gene therapy; phosphorothioate backbone
                                                                                                                                                                                                                                                                  Example 13; Page 95-107; 116pp; English
                                                                                          2001WO-US28572.
                                                                                                                 2000US-0663834
                                                                                                                                                               Cowsert LM
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                                                                                                                                                                                   WPI; 2002-471192/50.
N-PSDB; AAD38904.
                                              WO200222636-A1
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                                                                                                                                                               Bennett CF,
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                IQEFAGCKKI FGSLAFLPESFDGDPASNTAPLQPEQLQVFETLEEITGYLYISAWPDSLP
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                                             DLSVFQNLQVIRGRILHNGAYSLTLQGLGISWLGLRSLRELGSGLALIHHNTHLCFVHTV
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                                                      Gaps
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                          Length 1255;
                                                      IndelB
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                         DB
                         Score 4900; DB
Pred. No. 0;
0; Mismatches
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                         96.5%;
                                       al Similarity 73.2
919; Conservative
1255 AA;
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Human, Her-2, epidermal growth factor receptor 2; infection; cancer, hyperproliferative disorder; prophylaxis; inflammation; antisense;

protein.

Human Her-2 23-SEP-2002

AAE24067

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VNYLSTDVGSCTLVCPLHNQEVTAEDGTQRCEKCSKPCARVCYGLGMEHLREVRAVTSAN 360
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                                                                                                                                                                                                                                                                                           Disclosure; Page 114-117; 129pp; English.
                                                                                                                                                             Foy TM,
                                                                                                                                                             Cheever MA,
                                                                   14-AUG-2000; 2000US-225152P.
28-SEP-2000; 2000US-236428P.
21-FEB-2001; 2001US-270520P.
                                        14-AUG-2001; 2001WO-US41733
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Query Match
Best Local Similarity 73.2
Matches 919; Conservative
                                                                                                                                                           Hand-zimmermann S, Chee
Mcneill PD, Vedvick TS;
                                                                                                                               (CORI-) CORIXA CORP.
                                                                                                                                                                                                      2002-280758/32.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         1255 AA;
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1021..1030
/note= "Naturally processed HLA-B44-restricted epitope"
                PWDQLFRNPHQALLHTANRPEDECVGEGLACHQLCARGHCWGPGPTQCVNCSQFLRGQEC
                                                                           AGSDVFDGDLGWGAAKGLQSLPTHDPSPLQRYSBDPTVPLPSBTDGYVAPLFCSPQPEYV
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                                                        VEECRVLQGLPREYVNARHCLPCHPECQPQNGSVTCFGPEADQCVACAHYKDPPFCVARC
                                                                                                                 PSGVKPDLSYMPIWKFPDEEGACQPCPINCTHSCVDLDDKGCPAEQRASPLTS-----
                                                                                                                                                                                                                                                                                                                             781 YVSRLLGICLTSTVQLVTQLMPYGCLLDHVRENRGRLGSQDLLNWCMQIAKGMSYLEDVR
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The invention relates to an isolated Her-2/Neu polypeptide composition effective for eliciting an immune response. The invention is useful for eliciting an immune response. The invention is useful for eliciting an immune response. The invention is useful for the therapy and diagnosis of cancer. The composition is useful for the therapy and diagnosis of cancer. The compositions for the diagnosis, prevention and treatment of cand other compositions for the diagnosis, prevention and treatment of thuman malignancies, for stimulating and/or expanding T cells specific for Her-2/Neu polypeptide and for inhibiting the development of cancer in a companient. The invention is useful for stimulating a T cell response in a companient, as probe or primer for nucleic acid hybridisation, to selectively form duplex molecules with complementary stretches of the companient of selectively form a suitable library, and to direct expression of a length gene from a suitable library, and to direct expression of a prophylactic or therapeutic applications and for the treatment of cancer, correcterably for the immunotherapy of breast cancer and other Her-2/Neu cassociated malignancies. The invention is useful in gene therapy. The present sequence is human Her-2/neu protein.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          ELTYLPTNASLSFLQDIQEVQGYVLIAHNOVROVPLORLRIVRGTQLFEDNYALAVLDNG
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    1 MELAALCRWGLLLALLPPGAASTQVCTGTDMKLRLPASPETHLDMLRHLYQGCQVVQGNL
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                                                                                                                                                                                                                                                        Kalos MD;
                                                                                                                                                                                                                                                                                                                                                                                      Novel isolated Her-2/Neu polypeptide composition useful for t
prevention and diagnosis of cancer, preferably breast cancer
                                                                                                                                                                                                                                                          Lodes MJ,
WO200214503-A2
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/note= "intracellular domain"
990..1255
/note= "phosphorylation domain"

1..653
/note= "extracellular domain"
676..1255

Location/Qualifiers

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Her-2/neu fusion protein for treating or preventing cancer by or enhancing an immune response to the protein, has Her-2/neu extracellular domain fused to Her-2/neu intracellular or
                                                                                                                                                                                                   CORIXA CORP. SMITHKLINE BEECHAM BIOLOGICALS.
                                                                                                                                                                               33-AUG-2000; 2000US-0632507.
                                                                                                                                                          03-AUG-2001; 2001WO-US24283
                                                                                                                                                                                                                                                                                                                       phosphorylation domain
                                                                                                                                                                                                                                                       WPI; 2002-241743/29.
                                                                                                                                                                                                                                                                   N-PSDB; ABA92250.
                                                                                                                 WO200212341-A2.
           Homo sapiens.
                                                                                                                                                                                                                                   Cheever MA,
                                                                                                                                      14-FEB-2002
                                                                                                                                                                                                   (CORI-)
                                         Domain
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EEYLVPQQGFFCPDPAPGAGGWVHRRRSSSTRSGGGDLTLGLEPSEEEAPRSPLAPSEG 1080
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                                                      DLSVFQNLQVIRGRILHNGAYSLTLQGLGISWLGLRSLRELGSGLALIHNTHLCFVHTV
                                                                                                                                       PWDQLFRNPHQALLHTANRPEDECVGEGLACHQLCARGHCWGPGPTQCVNCSQFLRGQEC
                                                                                                                           VEECRVLQGLPREYVNARHCLPCHPECQPQNGSVTCFGPEADQCVACAHYKDPPFCVARC
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IQEFAGCKKIFGSLAFLPESFDGDPASNTAPLQPEQLQVFETLEEITGYLYISAWPDSLP
            IQEFAGCKKIFGSLAFLPESFDGDPASNTAPLOPEQLOVFETLEEIIGYLYISAWPDSLP
                                         DLSVPQNLQVIRGRILHNGAYSLTLQGLGISWLGLRSLRBLGSGLALIHHNTHLCFVHTV
                                                                                  PWDQLFRNPHQALLHTANRPEDECVGEGLACHQLCARGHCWGPGPTQCVNCSQFLRGQEC
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Gheysen D;

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The present sequence is that of human Her-2/neu (p185 glycoprotein or c-erbB2), an oncogenic self-protein and target for anti-cancer vaccines. The Her-2/neu gene is amplified and p185 is overexpressed in a variety of cancers, including breast, ovarian, colon, lung and prostate cancer. Her-2/neu is a member of the tyrosine kinase family of receptor-like glycoproteins. It comprises an extracellular comain with homology to the epidermal growth factor receptor (EGFR), a highly hydrophobic transmembrane domain and a C-terminal intracellular domain that also shows homology to EGFR. Its intracellular domain that also shows homology to EGFR. Its coveragession correlates with a poor prognosis in breast and overage sion correlates with a poor prognosis in breast and overage the fusion proteins or nucleic acids molecules. The invention provides Her-2/neu fusion proteins or nucleic acid molecules. In preferred fusion proteins, the extracellular domain or protein is fused to a Her-2/neu intracellular domain or
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        ELTYLPTNASLSFLQDIQEVQGYVLIAHNQVRQVPLQRLRIVRGTQLFEDNYALAVLDNG 120
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               phosphorylation domain (or its DeltapD fragment). An immune response to Her-2/neu protein is elicited or enhanced by administering the fusion protein in the form of a vaccine, or by transfecting cells of an animal avivo with a nucleic acid encoding the fusion protein, and delivering the transfected cells to the animal. The fusion proteins, nucleic acids, and isolated specific T-cells are useful for inhibiting the development of a cancer, especially breast, ovarian, colon, lung or prostate cancer in a patient. T cells that specifically react with a Her-2/neu fusion protein can be used to remove tumour cells from a sample in
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   Indels 336;
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Pred. No. 0;
0; Mismatches
Claim 68; Fig 7; 141pp; English.
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Best Local Similarity 73.2
Matches 919; Conservative
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Her-2/neu; oncogene; cancer; tumour; vaccine; human; p185; tyrosine kinase; receptor; c-erbB2; gene therapy.

Human Her-2/neu oncogene-encoded p185 glycoprotein.

17-JUN-2002

AAM51143;

AAM51143 standard; Protein; 1255 AA

RESULT 11 AAM51143

Oy 865 GGAAPQPHPPPAFSBAFDNLYYWDQDPPERCAPPSTFKGTPTAENPEYLGLDVPV 919 	RESULT 12 AAU77114 ID AAU77114 standard, Protein; 1255 AA.	XX AC AAU77114; XX XX DT 05-JUN-2002 (first entry)				PD 21-FEB-2002. XX PF 13-AUG-2001; 2001WO-US25408.	PR 14-AUG-2000; 2000US-0638280. PR 28-SEP-2000; 2000US-0675904. XX PA (CORI-) CORIXA CORP.	Gaiger A	DR WPI; 2002-280741/32. DR N-PSDB; ABK10730.	A. Inhibiting haematological malignancy development by administering PT polypeptide comprising immunogenic portion of Her-2/neu, polynucleotide PT encoding the polypeptide, or antigen presenting cells expressing the PT polypeptide.	PS Disclosure; Page 71-74; 74pp; English.	XX XX XX C The invention relates to a method for inhibiting development of CC haematological malignancy in a patient by administering a polypeptide CC comprising an immunogenic portion of Her-2/neu or a polynucleotide CC encoding the polypeptide. Antigen presenting cells that express the CC protein can also be administered. The sequences are used for inhibiting			Query Match 96.5%; Score 4900; DB 23; Length 1255; Best Local Similarity 73.2%; Pred. No. 0; Marches 919; Conservative 0; Mismatches 0; Indels 336; Gaps 1;	OY 1 MELAALCRWGLLIALLPPGAASTQVCTGTDMKLRLPASPETHLDMLRHLYQGCQVVQGNL 60	Qy 61 ELTYLPTNASLSFLQDIQEVQGYVLIAHNQVRQVPLQRLRIVRGTQLFEDNYALAVLDNG 120	Qy 121 DPLANNTTPVTGASPGGLRELQLRSLTEILKGGVLIQRNPQLCYQDTILWKDIFHKANQLA 180  121 DPLANNTTPVTGASPGGLRELQLRSLTEILKGGVLIQRNPQLCYQDTILWKDIFHKANQLA 180
61 ELTYLPTNASLSFLQDIQEVQGYVLIAHNQVRQVPLQRLRIVRGTQLFEDNYALAVLDNG 120 121 DPLANTTPVTGASPGGLRELQLRSLTEILKGGVLIQRNPQLCYQDTILWKDIFHKNNQLA 180 121 DPLANTTPVTGASPGGLRELQLRSLTEILKGGVLIQRNPQLCYQDTILWKDIFHKNNQLA 180	181 LTLIDTNRSRACHPCSPMCKGSRCWGESSEDCQSLTRTVCAGGCARCKGPLPTDCCHEQC 240	241 AAGCTGPKHSDCLACLHFNHSGICELHCPALVTYNTDTFBSMPNPEGRYTFGASCVTACP 300	YNYLSTDVGSCTLVCPLHNQBVTAEDGTQRCEKCSKPCARVCYGLGMEHLREVRAVTSAN	301 YNYLSTDVGSCTLVCPLHNOEVTAEDGTORCEKCSKPCARVCYGLGMEHLREVRAVTSAN 360 361 IQEFAGCKKIFGSLAFLPESFDGDPASNTAPLQPEQLQVFETLEEITGYLXISAWPDSLP 420 361 IQEFAGCKKIFGSLAFLPESFDGDPASNTAPLQPEQLQVFETLEEITGYLYISAWPDSLP 420	421 DLSVFQNLQVIRGRILHNGAYSLTLQGLGISWLGLRSLRELGSGLALIHHNTHLCFVHTV 480 	481 PWDQLFRNPHQALLHTANRPEDECVGEGLACHQLCARGHCWGPGPTQCVNCSQFLRGQEC 540	PROQUE KNEHQALLHIANKEEDE VGEGLACHQULAKGHUMGEGEI QCVNCSQE EKGGEC *** VEEGRULGGLEREYVNARHCLECHPECOPONGSYTCFGBEADQCVACAHYKDPPFCVARC 	PSGVKPDLSYMPIWKFPDEEGACOPCPINCTHSCVDLDDKGCAEQRASPLTS	PSGVKPDLSYMFIWKFPDEEGACQPCPINCTHSCVDLDDKGCPAEQRASPLTSIISAVVG	654	721 RKVKVLGSGAFGTVYKGIWIPDGENVKIPVAIKVLRENTSPKANKEILDEAYVMAGVGSP 780	654	LVHRDLAARNVLVKSPNHVKITDFGLARLLDIDETEYHADGGKVPIKMMALESILRRRFT	901 HQSDVWSYGVTVWELMTFGAKPYDGIPARBIPDLLEKGERLPQPPICTIDVYMIMVKCWM 960	654	685 EEYLVPQQGFFCPDPAPGAGGWVHHRHRSSSTRSGGGDLTLGLEPSEEEAPRSPLAPSEG 744	745 AGSDVFDGDLGMGAAKGLQSLPTHDPSPLQRYSEDPTVPLPSETDGYVAPLTCSPQPEVV 804	805 NQPDVRPQPPSPRGPLPAARPAGATLERPKTLSPGKNGVVKDVFAFGGAVENPEYLTPQ 864 

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RESULT 13 AAY92620 ID. AAY92620 ID. AAY92620; XX. AC. AAY92620; XX DT 10-AUG-2000 (first entry) XX DE Human heregulin 2 (Her2). XX KW Heregulin 2; Her2; vaccination; cytotoxic T-lymphocyte immunity; KW self-protein; cancer; breast cancer; prostate cancer; KW cell-associated peptide antigen; foreign epitope. XX	Key Domain Region Region	Region (133117 (148117 (148117 (148117 (148118118118118118118118118	Region 2 Domain 3 Region 3	FT Region 465479 FT Region /label= insertion region FT /note= "suitable for foreign epitope insertion" FT /label= Cysteine_rich_domain FT Region 579593 FT /label= insertion region FT /note= "suitable for foreign epitope insertion" FT /label= Transmembrane_domain FT /label= Transmembrane_domain	
181 LTLIDTNRSRACHPCSPMCKGSRCWGESSEDCQSLTRTVCAGGCARCKGPLPTDCCHEQC 240	421 DLSVFQNLQVIRGRILHNGAYSLTLQGLGISWLGLRSLRELGSGLALIHHNTHLCFVHTV 480 [	VEECRVIÇĞI PREYVNARHCI PCHPECOPONGSYTCFGBEADOCVACAHYKÖPPPECVARC. PSGVKPDLSYMPIWKFPDEGACOPCPINCTHSCVDLDDKGCPAEQRASPLTS PSGVKPDLSYMPIWKFPDEEGACOPCPINCTHSCVDLDDKGCPAEQRASPLTSIISAVVG	1 RKVKVLGSGAFGTVYKGIWI PDGENVKI PVAI KVLRENTSPKANKEILDEAYVMAGVGSP 4	901 HQSDVWSYGVTVWELMTFGAKPYDGIPAREIPDLLEKGERLPQPPICTIDVYMIMVKCWM 960 654	AGSDVFDGDLGMGAAKGLQSLPTHDPSPLQRYSEDPTVPLPSETDGYVAPLTGSPQPEYV

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241 AAGCTGPKHSDCLACLHFNHSGICELHCPALVTYNTDTFESMPNPEGRYTFGASCVTACP 300
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                                                           YNYLSTDVGSCTLVCPLHNQEVTAEDGTQRCEKCSKPCARVCYGLGMEHLREVRAVTSAN
                                                                                                                                  IQEFAGCKKIFGSLAFLPESFDGDPASNTAPLQPEQLQVFETLEEITGYLYISAWPDSLP
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    This is the human heregulin 2 (Her2) sequence. Immunogenic analogues of Her2 can be used in the claimed method as an autovaccine to induce a CTL response. Subdominant CTL epitopes, antibody binding regions and cysteine residues involved in disulfide bonds are preserved in the immunogenized forms. Regions suitable for the insertion of foreign T helper epitopes were identified (see features table). The method comprises including immune responses against weakly immunogenic cell-associated peptide antigens (PA) such as those associated with cancers (self-proteins), e.g. human prostate specific membrane antigen (PSM), heregulin 2 (Her2) and/or fibroblast growth factor 8b (FGPBb). The method comprises effecting simultaneous presentation by antigen (PSM), heregulin 2 (Her2) and/or fibroblast growth factor 8b (FGPBb). The method comprises effecting simultaneous system of: (1) at least 1 producting cell group derived from the PA and/or at least 1 B-cell group derived from the cell-associated PA; and (2) at least 1 B-cell group derived from the CTL and B-cell epitopes of the respective part of all known and predicted CTL and B-cell epitopes of the respective part of all known and predicted CTL and B-cell epitopes are also claimed. The method is used to treat prostate, prostate/breast or breast cancer when the PA is human PSM, FGF8b and Her2, respectively.
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Pred. No. 0;
0; Mismatches
                                                                            /label= C-terminal domain
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                                                                                                                                                                                                                                                                                                                      en S, Nielsen KG,
Karlsson G;
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ilarity 73.1%;
Conservative
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98US-0105011
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N-PSDB; AAA09455.
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es 918; Conser
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20-OCT-1998;
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541 VEECRVLQGLPREYVNARHCLPCHPECQPQNGSVTCFGPEADQCVACAHYKDPPFCVARC
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                                                         AGCTGPKHSDCLACLHFNHSGICELHCPALVTYNTDTFESMFNPEGRYTFGASCVTACP
                                                                                                                 YNYLSTDVGSCTLVCPLHNOEVTAEDGTORCEKCSKPCARVCYGLGMEHLREVRAVTSAN
                                                                                                                                   PWDQLFRNPHQALLHTANRPEDECVGEGLACHQLCARGHCWGPGPTQCVNCSQFLRGQEC
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  661 ILLVVVLGVVFGILIKRRQQKIRKYTMRRLLQETELVEPLTPSGAMPNQAQMRILKETEL
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                                     AAGCTGPKHSDCLACLHFNHSGICELHCPALVTYNTDTFESMPNPEGRYTFGASCVTACP
                                                                                                                                                                                          IQEFAGCKKI FGSLAFLPESFDGDPASNTAPLQPEQLQVFETLEEITGYLYISAWPDSLP
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                                                                                                                                                                                                                                                                                                                                                PWDQLFRNPHQALLHTANRPEDECVGEGLACHQLCARGHCWGPGPTQCVNCSQFLRGQEC
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          The invention relates to synthetic therapeutic compounds (antigenic peptides) with enhanced binding to major histocompatibility complex (MHC) molecules and enhanced immunoregulatory properties relative to their natural counterparts. Compounds of the invention are useful for inducting an immune response in a subject and for use in adoptive immunotherapy. They are useful as components of anti-cancer vaccines cimmunotherapy. They are useful as components of anti-cancer vaccines characterised by expression of the breast cancer antigen, HBR-2. Polynucleotides that encode peptides of the invention are useful as transcripts that are expressed in antigen presenting cells (APCs), to confirm transduction of polynucleotides inch observed in the present confirm transduction of polynucleotides inch observed in the present confirm transduction of polynucleotides inch observed in the present confirm transduction of polynucleotides inch observed in the HBR-2 antigenic peptide
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Novel synthetic therapeutic compound for inducing immune response and for use in adoptive immunotherapy, has enhanced binding to major histocompatibility molecules and enhanced immunoregulatory properties
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                                                                       Therapeutic compound, major histocompatibility complex; vaccine; antigenic peptide; MfC; immunoregulatory; immune response; HBR-2; adoptive immunocherapy; anti-cancer; breast cancer antigen; APC; antigen presenting cell; human; tyrosine kinase-type receptor.
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Pred. No. 0;
0; Mismatches
                                     Human tyrosine kinase-type receptor, HER-2.
                                                                                                                                                                                                        Location/Qualifiers
774..782
/note= "Antigenic epitope"
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Best Local Similarity 73.1%;
Matches 918; Conservative
                                                                                                                                                                                                                                                                                                                                                                  16-MAR-2001; 2001WO-US40328.
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(first entry)
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IQEFAGCKKIFGSLAFLPESFDGDPASNTAPLQPEQLQVFETLEEITGYLYISAWPDSLP
              PWDQLFRNPHQALLHTANR PEDECVGEGLACHQLCARGHCWGPGPTQCVNCSQFLRGQEC
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Treating tumors, particularly breast cancers, which overexpress an ErbB receptor and does not respond to an anti-ErbB antibody, comprises conjugating the antibody to a maytansinoid -
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   The present invention provides a method of treating cancer by administering a conjugate of anti-ErbB antibody with a maytansinoid. In particular, the antibody is directed against ErbB2 (also known as HER2 and p185neu). The method is particularly useful in the treatment of breast, ovarian, stomach, endometrial, salivary gland, lung, kidney, colon, colorectal, thyroid, pancreatic, prostate and bladder cancers.
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                                                                                                                          Human; HER2; ErbB2 receptor; p185neu; maytansinoid conjugate; cancer;
antibody.
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